PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 70025-9902	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US00/16396	International filing date *(day/month/year)* 15 JUNE 2000	Priority date *(day/month/year)* 12 AUGUST 1999
International Patent Classification (IPC) or national classification and IPC IPC(7): G01N 33/53; C07K 5/12 and US Cl.: 435/7.1, 4; 530/312, 317, 329, 330		
Applicant PALATIN TECHNOLOGIES, INC.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 0 sheets.

3. This report contains indications relating to the following items:

   I ☒ Basis of the report

   II ☐ Priority

   III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV ☒ Lack of unity of invention

   V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI ☐ Certain documents cited

   VII ☐ Certain defects in the international application

   VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09 MARCH 2001	28 DECEMBER 2001
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer MAURIE E. GARCIA Telephone No. (703) 308-0196

Form PCT/IPEA/409 (cover sheet) (July 1998)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/16396

I. Basis of the report

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-63 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 64-68 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-8 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This report has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

***Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/16396

IV. Lack of unity of invention

1. In response to the invitation to restrict or pay additional fees the applicant has:

- [ ] restricted the claims.
- [X] paid additional fees.
- [ ] paid additional fees under protest.
- [ ] neither restricted nor paid additional fees.

2. [ ] This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

- [ ] complied with.
- [X] not complied with for the following reasons:

Please See Supplemental Sheet.

4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:

- [X] all parts.
- [ ] the parts relating to claims Nos. _.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/16396

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	3-6, 9-17	YES
	Claims	1, 2, 7, 8	NO
Inventive Step (IS)	Claims	6	YES
	Claims	1-5, 7-14	NO
Industrial Applicability (IA)	Claims	1-17	YES
	Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Applicant's Response to Written Opinion filed 05 October 2001 has been considered and the arguments were found partially persuasive. Specifically, Applicant's arguments were found persuasive with respect to the novelty of claim 6 and the obviousness of claims 3-5 and 9-17 over the cited references. However, the statement regarding novelty for claims 1, 2, 7 and 8 over Sharma is maintained for the reasons set forth below.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., specific residues, structures) are not recited in the rejected claim(s). Although the claims are interpreted in light of the description, limitations from the specification are not read into the claims. Claims 1, 2, 7 and 8 contain no specific structure and the reference meets all of the recited limitations on the residues that make up the construct. Functional properties of these compounds would be inherent since the other limitations are met.

Also, Applicant argues that Sharma does not disclose compounds that are specific for melanocortin receptors. As set forth below, the examiner's position is that the reference does disclose compounds specific for these receptors in Example 44 in columns 48-49 and Example 54 in columns 52-53 (melanotropin analogues disclosed).

A new statement regarding the lack of inventive step for claims 3-5 and 9-17 has been set forth below with the incorporation of a new reference (ROYO et al).

Claims 1, 2, 7 and 8 lack novelty under PCT Article 33(2) as being anticipated by SHARMA (US 5,891,418).

Sharma discloses constructs that comprise N3S1 ligands that read directly on those claimed, see, for example, column 27, lines 6-65, especially lines 13-15. The ligands are made from tripeptides (three residues) and bind metal atoms. The reference discloses "peptide molecular constructs" that are specific for certain receptors. Specifically, Example 44 in columns 48-49 and Example 54 in columns 52-53 show melanotropin analogues.

(Continued on Supplemental Sheet.)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US00/16396

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to contain an adequate written description of the claimed constructs. The description is inadequate because of the following:
To satisfy the description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicants claim constructs (or libraries thereof) that are made of residues that are defined in functional terms. There are an unknown number of compounds that would fall within the claimed genus of constructs for the following reasons. The claims contain no specific structural information. The compounds in question could encompass widely varying structures. Also, it is unclear what the specific structure of the residues must be that make up the constructs of the claims in order to be encompassed by the claim limitations. Note that the goal of the description requirement is to clearly convey the information that an applicant has invented the subject matter which is claimed. Another objective is to put the public in possession of what the applicant claims as the invention so that the public may ascertain if the patent applicant claims anything that is in common use, or already known. The instant claims set forth only functional limitations on the residues that make up the construct and the instant description discloses only a very limited number of constructs. Adequate disclosure requires representative examples which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. The more unpredictable the art the greater the showing required (e.g. by representative examples) for adequate disclosure. The instant case deals with art that is highly unpredictable. Thus, it is deemed that the disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus. Moreover, the claimed genus encompasses members which are yet to be prepared or envisioned. This further evidences that the structural features of the exemplified constructs do not constitute support for the claimed genus or a substantial portion thereof.

Claims 1-5 and 7-17 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not adequately described in writing, as required under PCT Rule 5.1(a)(iii), for the reasons set forth in the immediately preceding paragraph.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

IV. LACK OF UNITY OF INVENTION:

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2, and 13.3 is not complied with for the following reasons:

As applicant was previously notified this International Preliminary Examining Authority has found plural inventions claimed in the International Application covered by the claims indicated below:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s)1 and 6-8, drawn to construct-N3S ligand.
Group II, claim(s) 2 and 6-8, drawn to peptides.
Group III, claim(s) 3, 5, 9-16, drawn to combinatorial library.
Group IV, claims 4-5, 9-15 and 17, drawn to combinatorial library of peptide mimetics.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

R1-Lll-Aaa-Bbb-Ccc-R2
R1-Bbb-Aaa-Ccc-R2
R1-DDdd-Bfbb-Aaa-R3 and etc. as recited in claim 6

The claims are deemed to correspond to the species listed above in the following manner:

1-2, 6-8

The following claims are generic: 1 and 2

and it considers that the International Application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:

The inventions listed as Groups I, II, III and IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the compounds in each Groups do not contain the same technical features as each of the compounds are structurally different containing e.g., different peptides, metals or non-peptide or analogues of the peptides to form the construct of Group I or peptides of group II can have different modified structures(i.e., analogs). The constructs and peptides can be used for other purposes such as therapy or diagnosis of diseases as well mediated by the melanocortin peptides rather than to make the library as recited in Groups III and IV.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: each of the species do not contain a special technical features with respect to structure and/or modes of action or operation.

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

Claims 3-5 and 9-17 lack an inventive step under PCT Article 33(3) as being obvious over SHARMA, as set forth above, in view of GORDON et al and GALLOP et al and ROYO et al.

Sharma discloses constructs that read directly on those claimed, supra. Sharma lacks the specific teaching of making combinatorial libraries of such constructs.

However, it was well known in the art at the time of filing to make peptide and peptidomimetic combinatorial libraries. For example, Gordon et al teaches the rationale for creating large combinatorial libraries, the criteria for library design and the quantity/quality of diversity (see pages 1385-7). Specifically, the reference teaches that "when small-molecule leads for a target have been previously defined ... the notion of searching for more potent derivatives among libraries combinatorially enriched in specific pharmacophore analogs would be an obvious tactic to pursue" (page 1386, 1st column).

Also, Gallop et al teach designing libraries based on a lead peptide, including "synthetic chemical approaches" (see Section "C" beginning on page 1240). Specific methodology for synthesis of peptide libraries in solution or on solid supports was well known along with the use of protecting groups (see pages 1240-1246 of Gallop et al and pages 1388-1389 of Gordon et al, for example).

Moreover, Sharma teaches the various limitations set forth in the instant claims 9-12 and 15-17. See column 27 of Sharma, especially lines 31-65. Sharma sets forth the various moieties of the constructs and their substitutions. Note that amino acids with protecting groups are taught, especially protected cysteine, see column 27, lines 36-41.

Lastly, Royo et al teach an orthogonal protecting group for cysteine residues (see Abstract) that reads on the protecting group of the instant claims. The protecting group of the reference is specifically set forth for use in solid-phase synthesis and is orthogonal with other common protecting group strategies (Boc and Fmoc); see pages 1095-1097 of the reference.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to make combinatorial libraries as claimed of the "peptide molecular constructs" of Sharma based on the teachings of the reference directed at various substitution patterns and the teachings of Gordon et al and Gallop et al directed to combinatorial chemistry. It would have been additionally obvious to use an orthogonal protecting group for cysteine residues in such constructs, due to the fact that it was well known in the art that "the side chain of cysteine requires protection during the coupling steps in solid-phase peptide synthesis" as evidenced by Royo et al (see specifically page 1095, 1st paragraph). One would have been motivated to make a library in order to have a large number of compounds to screen for more active/potent members. One would have been motivated to orthogonally protect the side chain of cysteine in such library compounds to preserve the activity of the thiol function (see Royo et al, page 1095, 1st paragraph).

Claim 6 meets the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest the specific composition of the claim.

Claims 1-17 meet the criteria set out in PCT Article 33(4) for industrial applicability because the claimed compounds could be used in therapeutic and diagnostic applications and the claimed libraries could be used to identify lead compounds.

---------- NEW CITATIONS ----------

GALLOP et al. Applications of Combinatorial Technologies to Drug Discovery. 1. Background and Peptide Combinatorial Libraries. J. Med. Chem. 29 April 1994, Vol. 37, No. 9, pages 1233-1251. See entire document.

GORDON et al. Applications of Combinatorial Technologies to Drug Discovery. 2. Combinatorial Organic Synthesis, Library Screening Strategies, and Future Directions. J. Med. Chem. 13 May 1994, Vol. 37, No. 10, pages 1385-1401. See entire document.

ROYO et al. S-Phenylacetamidomethyl (Phacm): an Orthogonal Cysteine Protecting Group for Boc and Fmoc Solid-phase Peptide Synthesis Strategies. J. Chem. Soc. Perkin Trans I. 07 May 1995, Vol. 9, pp. 1095-1102. See entire document.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/16396

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : G01N 33/53; C07K 5/12
US CL : 435/7.1, 4; 530/312, 317, 329, 330

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/7.1, 4; 530/312, 317, 329, 330

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS Online, West
Terms: melanocortin receptors, N3S ligand(metal complex or metal-conjugate), alpha melanocyte stimulating hormone

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,891,418 A (SHARMA) 06 April 1999, col.27, lines 12-15; col. 28, lines 5-15; col. 48, Example 44 up to col.49, line 60; col. 52,line 63 up to col. 53, line 17	1, 2, 6, 7, 8,
X,P	US 6,027,711 A (SHARMA) 22 February 2000, col. 20, lines 60 up to col. 21, line 7; col. 27, line 17; col. 34, line 62; col. 39, line 48 u p to col. 40, line 24.	1-17
A	US 5,690,905 A (ZAMORA et al) 25 November 1997, entire document.	1-17
A	US 5,200,504 A (GHADIRI) 06 April 1993, entire document	1-17
A	US 5,277,893 A (RHODES) 11 January 1994, entire document.	1-17

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 07 SEPTEMBER 2000	Date of mailing of the international search report 05 OCT 2000
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer T. WESSENDORF Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet) (July 1998)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/16396

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US00/16396

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1 and 6-8, drawn to construct-N3S ligand.
Group II, claim(s) 2 and 6-8, drawn to peptides.
Group III, claim(s) 3, 5, 9-16, drawn to combinatorial library.
Group IV, claims 4-5, 9-15 and 17, drawn to combinatorial library of peptide mimetics.
The inventions listed as Groups I, II, III and IV do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the compounds in each Groups do not contain the same technical features as each of the compounds are structurally different containing e.g., different peptides, metals or non-peptide or analogues of the peptides to form the construct of Group I or peptides of group II can have different modified structures(i.e., analogs). The constructs and peptides can be used for other purposes such as therapy or diagnosis of diseases as well mediated by the melanocortin peptides rather than to make the library as recited in Groups III and IV.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

R1-Lll-Aaa-Bbb-Ccc-R2
R1-Bbb-Aaa-Ccc-R2
R1-DDdd-Bfbb-Aaa-R3 and etc. as recited in claim 6

The claims are deemed to correspond to the species listed above in the following manner:

1-2, 6-8

The following claims are generic: 1 and 2

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: each of the species do not contain a special technical features with respect to structure and/or modes of action or operation.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

FILE COPY

To:
STEPHEN A. SLUSHER
PEACOCK, MYERS & ADAMS, P. C.
P. O. BOX 26927
ALBUQUERQUE, NM 87125-6927

PCT

INVITATION TO PAY ADDITIONAL FEES

(PCT Article 17(3)(a) and Rule 40.1)

Applicant's or agent's file reference 70025-PCT-16	Date of Mailing *(day/month/year)* **PAYMENT DUE** within 15 days from the above date of mailing
International application No. PCT/US02/25574	International filing date *(day/month/year)* 12 August 2002 (12.08.2002)
Applicant PALATIN TECHNOLOGIES, INC.	

1. This International Searching Authority

(i) considers that there are 10 *(number of)* inventions claimed in the international application covered by the claims indicated below/on an extra sheet:
Please See Continuation Sheet

and it considers that **the international application does not comply with the requirements of unity of invention** (Rules 13.1, 13.2 and 13.3) for the reasons indicated below/on an extra sheet:
Please See Continuation Sheet

(ii) ☐ has carried out a partial international search (see Annex) ☒ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.: 1-35

(iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid.

2. The applicant is hereby **invited**, within the time limit indicated above, to pay the amount indicated below:

$210.00	X 9	= $1,890.00
Fee additional per invention	number of additional inventions	total amount of additional fees

The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☐ Claim(s) Nos. _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Maurie G. Baker Telephone No. 703-308-1256

Form PCT/ISA/206 (July 1992)

INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/US02/25574

FILE COPY

This International Search Authority has found 10 inventions claimed in the International Application covered by the claims indicated below:
This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-35, drawn to a method of deriving a peptidomimetic of a biologically active metallopeptide.

Group II, claim(s) 36 and 37, drawn to a peptidomimetic comprising a template space.

Group III, claim(s) 38-40, drawn to a biologically active peptidomimetic.

Group IV, claim(s) 41-51, drawn to a peptidomimetic.

Group V, claim(s) 52-63, drawn to a second method of deriving a peptidomimetic of a biologically active metallopeptide.

Group VI, claim(s) 64-68 (in part), 69 and 73, drawn to a melanocortin receptor-specific peptidomimetic of a particular formula (i.e. claim 69).

Group VII, claim(s) 64-68 (in part), 70 and 74, drawn to a melanocortin receptor-specific peptidomimetic of a particular formula (i.e. claim 70).

Group VIII, claim(s) 64-68 (in part) and 71, drawn to a melanocortin receptor-specific peptidomimetic of a particular formula (i.e. claim 71).

Group IX, claim(s) 64-68 (in part) and 72, drawn to a melanocortin receptor-specific peptidomimetic of a particular formula (i.e. claim 72).

Group X, claim(s) 75-97, drawn to a method of deriving a peptidomimetic that binds to a target of interest.

1. This International Searching Authority considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated below:
The inventions listed as Groups I - X do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The technical feature that links some of the claims are the claimed "peptidomimetics". The groups lack unity because the claimed "peptidomimetics" are *known in the art* as disclosed by DiMaio et al (J. Chem. Soc. Perkin Trans. 1, 1989, pp. 1687-1689). This reference is discussed below.

DiMaio et al disclose a peptidomimetic compound that reads directly on those of claims 34, 35, 36, 37, 38 and 41. See compound denoted (2) in Scheme 1. Note that in this compound, the moiety denoted "Ar" refers to the side chain of tyrosine.

Also, various groups of the claims have no technical feature in common. For example, each of the products of Groups VI - IX have a *different chemical structure* and their modes of action and chemical reactivity would be different. Thus, they each represent separate and distinct products (having different inventive concepts). They differ in respect to their properties, the synthetic methodology for making them and/or their use.

See 37 CFR § 1.475 Unity of invention before the International Searching Authority, the International Preliminary Examining Authority and during the national stage, cited in part below (especially sections (c) and (d)).

(a) An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept (requirement of unity of invention). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression special technical features shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

(b) An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories:

product and a process specially adapted for the manufacture of said product; or

product and process of use of said product; or
product, a process specially adapted for the manufacture of the said product, and a use of the said product; or
process and an apparatus or means specifically designed for carrying out the said process; or
product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

(c) If an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b) of this section, unity of invention might not be present.

(d) If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and § 1.476(c).

The instant international application contains multiple products and methods, where the feature that links the claims is known in the art, as set forth above. Thus, the instant claims lack unity of invention.